REMARKS

Claims 1 and 3 are pending after entry of this paper. Claims 2 and 4 have been canceled without prejudice. Applicants reserve the right to pursue the subject matter of the canceled claims in one or more continuing or divisional applications.

Claims 1 and 3 have been amended to incorporate the subject matters of claims 2 and 4, respectively. No new subject matter has been introduced by these amendments and support can be found throughout the specification and claims as filed. Amendments have been made solely to further prosecution and expedite allowance of the instant application. Applicants respectfully request reconsideration in view of the claim amendments and the following remarks.

Response to Specification Objection

The Examiner contends that the title of the invention is not descriptive and has requested a new title. Applicants have addressed this concern in the "Amendments to the Title" section above.

The Examiner notes "that the proper designation of 'cdl' is 'CD40L'" on page 2 of the Office Action, however, the Examiner does not cite any use of "cdl" in the instant application. Applicants are unaware of any instance where the use of "cdl" is found in the instant specification or claims. Applicants believe that the proper designation of "CD40L" has been used throughout the application and are, therefore, unable to address the Examiner's concern regarding this point. Applicants respectfully request that the Examiner specifically point to the objected occurrences of "cdl".

On page 2 of the Office Action, the Examiner notes that "the antagonist should be spelled 'antagonist'". Applicants note that in the published version of the application, the title is misspelled. Applicants respectfully direct the Examiner's attention to the application as filed which was submitted with the proper spelling of the word "antagonist". Applicants are unaware of any other instance where the word "antagonist" is misspelled in the instant application. Applicants believe that the term "antagonist" has been spelled correctly throughout the application and are, therefore, unable to address

the Examiner's concern regarding this point. Applicants respectfully request that the Examiner specifically point to the objected occurrences of "antagonist".

The Examiner contends that trademarks appearing in the specification are used inappropriately; however, the Examiner does not specifically point to any use (or misuse) of trademarks in the instant application (see Office Action, page 2). Applicants have reviewed the application and cannot find an instance where a trademark is being used. Therefore, applicants are unable to correct or address the Examiner's concern regarding this point. Applicants respectfully request that the Examiner specifically point to the objected use or misuse of trademarks.

Additionally, amendments to the specification are provided to correct spelling and grammatical errors which were inadvertently submitted with the application. No new matter has been introduced with the amendments and support can be found throughout the instant invention and claims as filed. Applicants believe that the above-mentioned amendments address the Examiner's concerns.

In view of the above mentioned amendments and remarks, applicants respectfully request reconsideration and withdrawal of the objections to the claims and specification.

Response to 35 U.S.C. §112, Second Paragraph Rejection

Claims 1-4 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically, the Examiner states in the instant Office Action that the recitations of "a CD40L receptor" and "a CD40 receptor" are indefinite, because the nature of these receptors is ambiguous.

Applicants have canceled claims 2 and 4, rendering the rejection to these claims now moot. Additionally, claims 1 and 3 have been amended to delete the recitations "a CD40L receptor" and "a CD40 receptor." Applicants believe that the above mentioned amendments to the claims address the Examiner's concerns.

In view of these amendments, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph to claims 1-4 are respectfully requested.

Response to 35 U.S.C. §112, First Paragraph Rejection

Claims 3 and 4 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (Office Action, page 3). Claim 4 has been canceled and the subject matter of the claim has been incorporated into claim 3. Therefore the rejection to claim 4 is now moot. However, applicants respectfully disagree with the rejection to claim 3 and traverse the rejection as follows.

Firstly, the Examiner states in the outstanding Office Action on page 3 that:

> [s]ince the therapeutic indices of immunosuppressive drugs or biopharmaceutical drugs can be species- and model-dependent, it is not clear that reliance on the in vitro and in vivo experimental observations as well as the clinical experience with targeting various inflammatory conditions with CD40L-specific antibodies accurately reflects the relative ability or efficacy of the claimed 'preventative agents' to prevent pemphigus.

Applicants respectfully disagree with the Examiner's contentions and direct the Examiner to page 1, lines 13-15 of the specification, which states "that pemphigus is induced by autoantibodies against desmoglein (Dsg) which is a cadherin-type cell adhesion molecule found in desmosome." One skilled in the art would understand that a mouse would be an appropriate model system for studying the claimed invention, because the pathogenic mechanism of pemphigus induced by autoantibodies against Dsg is commonly shared by human and mouse. Furthermore, according to the MPEP guidelines, human trials are not required by an applicant to demonstrate enablement. Applicants respectfully direct the Examiner's attention to MPEP §2107.03 (III) which states that "[d]ata from *in vitro* or animal testing is generally sufficient to support therapeutic utility." Additionally, MPEP §2107.03 (V) states that "[o]ffice personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials." Thus, according to the MPEP guidelines the working example

provided by the applicants, *i.e.*, use of the mouse model system, is sufficient in demonstrating enablement.

Applicants assert that one skilled in the art understands from reading Example 2 and Figure 1 of the specification that the administration of a CD40L antibody (*i.e.*, MR1) would be effective as a preventive agent for pemphigus. Example 2 describes that the MR1 antibody and the control hamster IgG were intraperitoneally administered to recipient mice ($Rag2^{-/-}$ mice) (n=5) two days before the transfer of $Dsg3^{-/-}$ mouse splenocytes and 0, 2, 4 and 7 days after the transfer. In the control mice, anti-Dsg3 antibody was found; however, even after 66 days, the MR1 treated mice did not result in apparent anti-Dsg3 antibody production. Moreover, only the control mice, and not the MR1 treated mice, were observed to have weight loss and other pemphigus related characteristics. Therefore, the applicants assert that the claims are fully enabled by the disclosure in the specification for the skilled artisan to make and use the claimed invention, specifically the use of an anti-CD40L antibody for preventing pemphigus.

Secondly, in the Office Action on page 3, the Examiner points out that "[p]harmaceutical therapies in the absence of *in vivo* clinical data are unpredictable". However, this point is not understood, because the experimentation in Example 2 and Figure 1 of the specification is an *in vivo* experiment where an anti-CD40L antibody was administered into mice. If, in fact, the Examiner is concerned that human clinical trials have not been performed, applicants again direct the Examiner to MPEP §2107.03 as indicated in the previous paragraph.

Thirdly, the Examiner contrasts the nature of human disease as "chronic" with that of animal models as "acute," and concludes that "the treatment of pemphigus is drawn to the treatment of the disease and its associated lesions subsequent to an individual being diagnosed with pemphigus and not as a preventative agent of the disease itself, as recited in the current claims" (Office Action- page 4). The Examiner's point is that the treatment of pemphigus is not possible until its development, and therefore its prevention is impossible. Applicants respectfully disagree with the Examiner's contention. Applicants direct the Examiner to Starzycki, et al. ("Familial pemphigus vulgaris in mother and daughter". *International Journal of Dermatology*. 37(3):211-214, March 1998.; "Starzycki reference"; abstract submitted herewith) and

Katzenelson, et al. ("Familial pemphigus vulgaris". *Dermatologica*. 1990;181(1):48-50; "Katzenelson reference"; abstract submitted herewith). These references show that at the time the instant application was filed, it was known in the art that familial cases of pemphigus exist, which demonstrates that certain people are predisposed to the disease. Interestingly, the Katzenelson reference states that a "woman and her son developed the disease within a period of 18 months from one another," which suggests that there was a possibility to prevent the disease from developing in the second person. Additionally, Tur, et al. ("Diet and pemphigus. In pursuit of exogenous factors in pemphigus and fogo selvagem". *Arch Dermatol*. 1998 Nov;134(11):1406-10.; "Tur reference"; abstract submitted herewith) describe exogenous factors which play a role in pemphigus development which further demonstrates that certain people (*i.e.,* people who are exposed to these factors) are predisposed to developing pemphigus. Therefore, since it is known in the art that certain people are predisposed to this disease, one skilled in the art would appreciate that there are instances where it would be useful to utilize the instant invention to prevent the onset of the pemphigus.

Furthermore, the instant invention could be utilized to prevent the reoccurrence of the disease. Consider a patient who has been diagnosed with pemphigus but later recovered with a remedy. While this patient currently is not diagnosed as having pemphigus, this patient has a predisposition to pemphigus and the risk of its recurrence is high. In this case, it is quite rational to prevent the recurrence of pemphigus with the preventive agent of the invention.

For the reasons stated above, at the time of the invention, one skilled in the art would have considered that the claimed preventive agent of pemphigus does not necessitate undue experimentation to use and/or make the same, and would be enabled to practice the claimed invention. Reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph are respectfully requested.

Claims 1 and 3 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the

Examiner asserts in the outstanding Office Action that "there is insufficient written description of the broadly recited 'antagonists' or 'agents' in the absence of a sufficient description showing possession of the necessary functional characteristics coupled with a known or disclosed correlation between function and structure" (page 5).

Applicants respectfully disagree with the Examiner's contention, however in order to expedite prosecution and solely for the allowance of the instant application, applicants have amended claims 1 and 3. Claims 1 and 3 have been amended to replace the term "an antagonist" with "an anti-CD40L antibody." No new matter has been introduced with this amendment and support can be found throughout the specification as filed, for example in paragraph 2, page 6, Example 2 and Figure 2. Applicants assert that it is clear from Example 2 and Figure 2 of the specification that the inventors were in possession of an anti-CD40L antibody and methods of use as claimed at the time of the application filing.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph in view of the above mentioned amendments and remarks.

Response to 35 U.S.C. §102 Rejection

Claims 1-4 have been rejected under 35 U.S.C. §102(b) as being anticipated by Black, et al. (U.S. Patent No. 6,001,358).

Claims 2 and 4 have been canceled and the rejections to those claims are now moot. In order to expedite prosecution without disclaimer of or prejudice to the subject matter recited in the instant application, applicants have amended claims 1 and 3, such that they are directed to a remedy for or a preventive agent against pemphigus containing, as an active ingredient, an anti-CD40L antibody. Briefly, Black, et al. characterizes humanized antibodies to human gp39. In particular, Black, et al. do not disclose that an anti-CD40L antibody is effective in preventing pemphigus. In fact, Black does not provide any specific experimental data, either *in vitro* or *in vivo*, supporting the use of an anti-CD40L antibody as a remedy for or a preventive agent against pemphigus. Applicants respectfully direct the Examiner's attention to Black at column 32, line 21 - column 33, line 22 which lists several conditions which are

"potentially treatable," including pemphigus. Applicants assert that the Examiner has used hindsight in selecting pemphigus out of a laundry list of possible conditions, and there is nothing in Black, et al. to provide guidance as to how one would use the antibody for treating/preventing pemphigus. Specifically, applicants assert that:

> Just because a moiety is listed as one possible choice for one position does not mean there is ipsis verbis support for every species or subgenus that chooses that moiety. Were this the case, a "laundry list" disclosure of every possible moiety for every possible position would constitute a written description of every species in the genus. Fujikawa v. Watanasin, 93 F.3d 1559, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1996).

Moreover, as the Examiner is aware:

> [a] reference itself must have an enabling disclosure to be used as a proper reference. Section 102(b) of 35 U.S.C. and its predecessor statues have been interpreted as requiring the description of the invention in a publication to be sufficient to put the public in possession of the invention. *Ex parte Gould*, 231 U.S.P.Q. 943 (B.P.A.I. 1986).

The instant invention, supported by the specific experimental data of the working examples, can not be considered to be the same as the invention of Black, et al., which is only an armchair imagination. Plainly speaking, the invention of Black, et al. concerning treatment for and prevention of pemphigus is incomplete. It is illogical to say that a completed invention is the same as an incomplete invention. Therefore, applicants assert that Black does not anticipate the claimed invention because Black does not disclose a remedy for or a preventive agent against pemphigus. Reconsideration and withdrawal of the §102 rejection to claims 1-4 are respectfully requested for the above reasons.

Claims 1 and 3 have been rejected under 35 U.S.C. §102(b) as being anticipated by Armitage et al. (U.S. Patent No. 6,264,951). Applicants respectfully disagree with

the Examiner contention that Armitage discloses each and every element of the claimed invention.

Claims 1 and 3 have been amended to be directed to a remedy or a preventive agent for pemphigus containing, as an active ingredient, an anti-CD40L antibody. The Examiner admits on page 7 of the instant Office Action that "the prior art does not teach the intended use of such antagonists for pemphigus per se." However, in order to expedite prosecution without disclaimer of or prejudice to the subject matter recited in the instant application, applicants have amended the claims such that they are directed to an anti-CD40L antibody. Armitage, et al. do not disclose a remedy or a preventive agent for pemphigus containing, as an active ingredient, an anti-CD40L antibody. Therefore, applicants respectfully request reconsideration and withdrawal of the §102 rejection to claims 1-4 for the above claim amendments and reasons.

In view of these amendments and arguments, reconsideration and withdrawal of rejections to claims 1-4 under 35 U.S.C. §102 are respectfully requested.

CONCLUSION

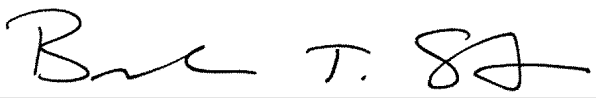
Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application. Favorable action by the Examiner is earnestly solicited.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 4439-4025.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 4439-4025.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: June 29, 2007 By: 

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